Claims

1. A method for the identification (or isolation or separation) of identical nucleic acid fragments from a mixture of at least two nucleic acid populations, comprising: a) separate digestion of the nucleic acids of said at least two populations with at least one restriction enzyme; b) ligation of an adaptor sequence to the restriction fragments; c) amplification of the adaptor-ligated restriction fragments generated in a) and b) using an adaptor-specific primer; d) hybridisation of the amplification products from the different nucleic acid populations with each other ; e) identification (or isolation or separation) of the fully matched heterohybrid fragments.

2. A method of claim 1, wherein the nucleic acid populations are genomic DNA populations, preferably human genomic DNA populations, more preferably from different subjects having a common trait of interest.

3. Method of claim 1 or 2, wherein the nucleic acid populations comprise selected chromosome(s).

4. Method of any one of claims 1 to 3, wherein two or more nucleic acid populations from different sources are used.

5. Method according to any one of the preceding claims, wherein the restriction fragments are size selected prior to the amplification reaction.

6. Method according to any one of the preceding claims, wherein part or all of the restriction fragments are cloned into a vector, in a chromosome- and sequence-specific fashion.

7. Method according to any one of claims 1 to 6, wherein the adaptor sequence comprises a recognition site for *mut* HL.

8. Method of claim 7, wherein the adaptor molecule is a 5-100 base long double-stranded DNA fragment comprising at least one GATC motif.

9. Method according to any one of claims 1 to 8, wherein the amplification is a by polymerase chain reaction (PCR).

10. Method according to any one of claims 1 to 9, wherein the primer is complementary to at least a part of the adaptor molecule sequence.

11. Method of claim 9, wherein the primer is labelled, preferably by (i) adding a unique 5'-sequence to each primer, (ii) adding a chemical activity to the primer which provides a means to distinguish between the amplification products from different nucleic acid populations or (iii) adding modified nucleotides into the primer allowing to distinguish between the amplification products from different nucleic acid populations.

12. Method according to any one of the preceding claims, wherein the identification of matched heterohybrids comprises a (i) separation of homoduplexes from heteroduplexes; (ii) (identification and) elimination of mismatched heterohybrids, and iii) identification (or isolation or separation) of the fully matched heterohybrid fragments.

13. Method of claim 12., wherein the heterohybrids are separated from the homohybrids based on labelling of primers.

14. Method of claim 13, comprising a) separate amplification of the restriction fragments using a primer with a unique 5' sequence for each nucleic acid population; b) mixing the amplification products from said

different nucleic acid populations carrying unique 5' ends; c) denaturation and rehybridizing said nucleic acids; d) digesting perfectly matched (blunt ended) DNA's (homoduplexes) by *Exo* III and e) elimination of the *Exo* III created single strands, preferably through binding to a single strand specific matrix.

15. Method of claim 12, wherein the heterohybrids are separated from the homohybrids based on the methylation of one of the two nucleic acid preparations (or restriction fragments).

16. Method of claim 12, wherein mismatched heterohybrids are eliminated with mismatch repair enzymes.

17. Method of claim 16, wherein mismatched nucleic acid fragments are eliminated by (i) incubating the hybridisation mixture with MutS and (ii) contacting the resulting product with a *Mut*S-binding material.

18. Method of claim 16, wherein mismatched nucleic acid fragments are eliminated by incubating the hybridisation mixture with *Mut*S, *Mut*L and *Mut*H, resulting in a specific cleavage of mismatched hybrids.

19. A kit suitable for genetic analysis in accordance with claim 1, comprising a double stranded adaptor molecule, a specific labelled primer and, optionally, control DNA's and enzymes.

20. Kit of claim 19, further comprising a means for the detection of the selected DNA fragments, preferably an ordered DNA array or coded beads carrying specific DNA sequences.

21. A method of separating identical DNA fragments from complex mixtures of at least two nucleic acid populations, comprising hybridizing the at least two populations and separating the fully

matched heterohybrids formed, wherein the nucleic acid populations comprise amplified nucleic acids.

22. A method to identify DNA regions that are relevant to a pathological condition or a particular trait, comprising hybridizing at least two nucleic acid populations from different sources having the particular trait or pathology, and separating the fully matched heterohybrids formed said fully matched heterohybrids containing DNA regions that are relevant to said pathological condition or particular trait, wherein the nucleic acid populations comprise amplified and/or pre-selected nucleic acids.